UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/633,145	08/04/2000	Chinnappa Kodira	CL000747	3253

7590 12/16/2002

Celera Genomics Corp.
Attn: Robert A. Millman, Patent Director
C2- 4 # 20
45 West Gude Drive
Rockville, MD 20850

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/633,145	KODIRA ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8,9,13 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,8,9 and 24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *19* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *20* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, since the fee set forth in 37 CFR 1.17(e) has been timely paid. Applicant's submission filed on 9 October 2002 (Paper 17) has been entered. The Preliminary Amendment and Information Disclosure Statement, sent 9 October 2002, have been entered as Papers 18 and 19, respectively. Claim 4 was amended. Claim 30 was added and reads on the elected Invention. Claim 13 has been withdrawn by the Examiner as being drawn to a non-elected Invention.

Claims 4, 8, 9 and 24-30 are under examination in the current application.

Claim Rejections/Objections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 8, 9 and 24-30 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to recombinant expression of the peptide encoded by SEQ ID NO: 2, the nucleic acids encoding SEQ ID NO: 2 and complementary nucleic acids.

No well-established utility exists for newly-isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed polypeptide and the polynucleotides and recombinant methods used to express it:

Each of these shall be addressed in turn:

1) For the production of antibodies;

2) To make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO: 2 and to localize receptor expression in tissue samples;

3) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide;

4) To produce a variant or chimeric nucleotide or polypeptide;

5) In the creation of transgenic animals;

6) To detect polymorphisms in individuals;

7) For clinical therapy using the polypeptide or ligand.

Each of these shall be addressed in turn:

1) For the production of antibodies. This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses

nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility.

2) To make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO: 2 and to localize receptor expression in tissue samples. This asserted utility is credible but not substantial or specific. Hybridization probes and primers can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide. This asserted utility is credible and specific. However, it is not substantial. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure for example, of how to assay for ligand binding and possible transduction mechanisms. It is not known the class of drugs to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial.

4) To produce a variant or chimeric nucleotide or polypeptide. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification discloses nothing specific or substantial for the variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present in

mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) In the creation of transgenic animals. This asserted utility is credible but not specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the present invention. Significant further experimentation would be required of the skilled artisan to identify such a disease. The specification discloses nothing about whether the claimed gene will be "knocked in" or "knocked out" or what specific tissues and cells are being targeted. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

6) To detect polymorphisms in individuals. This asserted utility may be credible, however it is neither specific nor substantial. Applicants have not demonstrated the function of the polypeptide encoded by the claimed polynucleotide, much less relevant polymorphisms. Thus, the asserted utility is not substantial. Finally, many unrelated sequences can be polymorphic, generally. Thus, the asserted utility is not specific.

7) For clinical therapy using the polypeptide or ligand. This asserted utility is credible but not specific or substantial. Such can be performed for any polypeptide. Further, the specification does not disclose diseases associated with the gene of the claimed invention or with the polypeptide encoded by the gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease and to determine the route of administration of the polypeptide or ligand, as well as quantity and duration of treatment. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Claims 4, 8, 9 and 24-30 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The disclosed polypeptide has high homology to the N-methyl-D-aspartate receptor, as shown in Figure 2 of the instant Specification (Sucher, N.J., 1999, Accession No. T31068). The specification likewise asserts that the claimed polynucleotide(s) encode receptors for biogenic amines. However, the specification does not teach functional or structural characteristics of the amine receptor polypeptide recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi-functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity.

Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to make a biologically active amine receptor-like polypeptide without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

Applicant's arguments (pp 4-6, Paper No. 18, 09 October 2002) have been fully considered but are not found to be persuasive for the following reasons.

The Information Disclosure Statement, submitted 9 October 2002 (Paper 19), gives examples of experiments in which the human trace amine receptor (TA_1) is shown to have distinct and specific ligand binding properties (Borowsky, et al, 2001, PNAS, 98: 8966-8971;

Bunzow, et al, 2001, Mol. Pharmacol. 60: 1181-1188; Kim, et al, 2001, Mol. Pharmacol. 60: 1165-1167). This appears to be inconsistent with the peptide disclosed in the instant Specification being a rat NMDA receptor, as shown in Figure 2. The fact that the claimed polypeptide appears to be an NMDA receptor, *and* has high homology to a trace amine receptor appears to be inconsistent. Furthermore the type of receptor disclosed by the Applicants is unclear since there are few details about specific function predicted from the Applicant's disclosure. The statements in the Amendment submitted 9 October 2002 (Paper 18) are not supported by data that can be independently evaluated by the examiner. Given the inconsistencies noted above, the conclusory statements cannot be accepted on their face.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide encoded by the claimed polynucleotides such that it can be determined how to use the claimed polynucleotides and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of

the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion: Claims 4, 8, 9, and 24-30 are rejected for the reasons listed above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

12/06/02

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER